Notice of Allowability	Application No.	Applicant(s)	
	09/582,404	YAMASHITA ET AL.	
	Examiner	Art Unit	
	Alton N. Pryor	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to *interview summary*.

2. ☐ The allowed claim(s) is/are *4,9,10,12,17-22 (claims renumbered 1-10)*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Synder on 12/20/04.

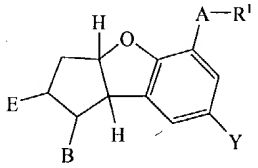
The application has been amended as follows:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-3. (Canceled).

Claim 4. (Currently amended) A sustained-release pharmaceutical composition ~~comprising~~ consisting essentially of an ionic prostaglandin I_2 derivative of the following general formula (I):



and an ionic compound having an opposite charge to that of the ionic prostaglandin I_2 derivative, which increases the oil/water partition coefficient of the ionic prostaglandin I_2 derivative,

wherein

R^1 represents $COOR^2$ (wherein R^2 represents:

1) hydrogen or a pharmacologically acceptable cation,
2) -Z-Ar^1, wherein Z is a valence bond or a straight or branched alkylene shown by C_tH_{2t} wherein t is an integer of 1 to 6, and Ar^1 is 2-pyridyl, 3-pyridyl or 4-pyridyl;

3) $-C_tH_{2t}COOR^3$, wherein C_tH_{2t} has the same significance as defined above, and R^3 is hydrogen or a pharmacologically acceptable cation;

or,

4) $-C_tH_{2t}N(R^4)_2$, wherein C_tH_{2t} has the same significance as defined above, and R^4 is hydrogen, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms);

A represents:

1) $-(CH_2)_m-$, wherein m is an integer of 1 to 3;
2) $-CH=CH-CH_2$;
3) $-CH_2-CH=CH-$;
4) $-CH_2-O-CH_2-$;
5) $-CH=CH-$;
6) $-O-CH_2-$; or,
7) $-C\equiv C-$;

Y represents hydrogen, an alkyl having 1 to 4 carbon atoms, chlorine, bromine, fluorine, formyl, methoxy or nitro;

B represents $-X-C(R^5)(R^6)OR^7$ (wherein R^5 represents hydrogen or an alkyl having 1 to 4 carbon atoms; R^7 represents hydrogen, an acyl having 1 to 14 carbon atoms, an aroyl having 6 to 15 carbon atoms, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl or t-butyl; X represents:

1) $-CH_2-CH_2-$;
2) $-CH=CH-$;or
3) $-C\equiv C-$;

R^6 represents:

1) a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms;
2) $-Z-Ar^2$ wherein Z has the same significance as defined above and Ar^2 is phenyl, α-naphthyl, β-naphthyl or a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an

alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy;

3) $-C_tH_{2t}OR^8$, wherein C_tH_{2t} has the same significance as defined above, and R^8 is a straight alkyl having 1 to 6 carbon atoms, a branched alkyl having 3 to 6 carbon atoms, phenyl, a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy, cyclopentyl, cyclohexyl, or a cyclopentyl or cyclohexyl substituted with 1 to 4 straight alkyl group(s) having 1 to 4 carbon atoms;

4) $-Z-R^9$, wherein Z has the same significance as defined above, and R^9 is hydrogen, a cycloalkyl having 3 to 12 carbon atoms or a substituted cycloalkyl having 3 to 12 carbon atom which is substituted with 1 to 3 alkyl groups having 1 to 5 carbon atoms;

5) $-C_tH_{2t}-CH=C(R^{10})R^{11}$, wherein C_tH_{2t} has the same significance as defined above, and R^{10} and R^{11} represent hydrogen, methyl, ethyl, propyl or butyl; or

6) $-C_uH_{2u}-C\equiv C-R^{12}$, wherein u is an integer of 1 to 7, C_uH_{2u} is a straight or branched alkylene and R^{12} is a straight alkyl having 1 to 6 carbon atoms);

E represents hydrogen or OR^{13}, wherein R^{13} is hydrogen, an acyl having 1 to 12 carbon atoms, an aroyl having 7 to 18 carbon atoms, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms; or a salt thereof, wherein the ionic compound is a compound containing a group selected from an ammonium, pyridinium, phosphonium and sulfonium group in the molecule thereof, or a salt thereof, or alternatively, a compound containing a carboxyl, sulfate, sulfonate or phosphate group in the molecule thereof, or a salt thereof, with optionally at least one additional component selected from the group consisting of vegetable oil, fatty acid triglycerides, fatty acid esters, polysiloxanes, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen, **~~wherein the ionic compound is~~**

~~incorporated at least in an equimolar amount based on the ionic prostaglandin I_2 derivative in terms of a charge ratio and wherein the ionic prostaglandin I_2 derivative is anionic~~.

Claim 5. (Canceled)

Claim 6. (Canceled)

Claim 7. (Canceled)

Claim 8. (Canceled)

Claim 9. (Previously presented) A sustained-release pharmaceutical composition according to claim 4, wherein the ionic compound contains at least one member selected from the group consisting of an alkyldimethylbenzylammonium salt, an alkyltrimethylammonium salt, an alkylpyridinium salt, an alkylamine salt and an alkylphosphonium salt.

Claim 10. (Original) A sustained-release pharmaceutical composition according to claim 9, wherein the ionic compound is benzalkonium chloride.

Claim 11. (Canceled)

Claim 12. (Previously Presented) A sustained-release pharmaceutical composition according to claim 4, wherein the prostaglandin I_2 derivative is (±)-(1R*-2R*, 3aS*, 8bS*)-2,3,3a,8b-tetrahydro-2-hydroxy-1-[(E)-(3D*)-3-hydroxy-4-methyl-1-octen-6-ynyl]-1H-cyclopenta[b]benzofuran-5-butanoic acid, or a salt thereof.

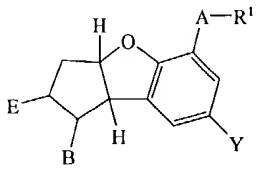
Claim 13. (Canceled)

Claim 14. (Canceled)

Claim 15. (Canceled)

Claim 16. (Canceled).

Claim 17. (Currently amended) A sustained-release pharmaceutical composition for an ~~cationic~~ ionic prostanoic acid derivative ~~comprising~~ consisting essentially of an prostanoic acid derivative and an ionic compound having an opposite charge to that of the ionic prostanoic acid derivative and increasing hydrophobicity of the prostanoic acid derivative, wherein said ionic compound contains a carboxyl, sulfate, sulfonate or phosphate group in the molecule thereof, or a salt thereof, and wherein said prostanoic acid derivative is of the formula:



wherein

R^1 represents $COOR^2$ (wherein R^2 represents:

1) hydrogen or a pharmacologically acceptable cation,
2) $-Z-Ar^1$, wherein Z is a valence bond or a straight or branched alkylene shown by C_tH_{2t} wherein t is an integer of 1 to 6, and Ar^1 is 2-pyridyl, 3-pyridyl or 4-pyridyl;
3) $-C_tH_{2t}COOR^3$, wherein C_tH_{2t} has the same significance as defined above, and R^3 is hydrogen or a pharmacologically acceptable cation;

or,

4) $-C_tH_{2t}N(R^4)_2$, wherein C_tH_{2t} has the same significance as defined above, and R^4 is hydrogen, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms);

A represents:

1) $-(CH_2)_m-$, wherein m is an integer of 1 to 3;
2) $-CH=CH-CH_2$;
3) $-CH_2-CH=CH-$;
4) $-CH_2-O-CH_2-$;
5) $-CH=CH-$;

6) -O-CH_2-; or,

7) C≡C-;

Y represents hydrogen, an alkyl having 1 to 4 carbon atoms, chlorine, bromine, fluorine, formyl, methoxy or nitro;

B represents -X-$C(R^5)(R^6)OR^7$ (wherein R^5 represents hydrogen or an alkyl having 1 to 4 carbon atoms; R^7 represents hydrogen, an acyl having 1 to 14 carbon atoms, an aroyl having 6 to 15 carbon atoms, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl or t-butyl; X represents:

1) -CH_2-CH_2-;

2) -CH=CH-;or

3) -C≡C-;

R^6 represents:

1) a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms;

2) -Z-Ar^2 wherein Z has the same significance as defined above and Ar^2 is phenyl, α-naphthyl, β-naphthyl or a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy;

3) -$C_tH_{2t}OR^8$, wherein C_tH_{2t} has the same significance as defined above, and R^8 is a straight alkyl having 1 to 6 carbon atoms, a branched alkyl having 3 to 6 carbon atoms, phenyl, a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy, cyclopentyl, cyclohexyl, or a cyclopentyl or cyclohexyl substituted with 1 to 4 straight alkyl group(s) having 1 to 4 carbon atoms;

4) -Z-R^9, wherein Z has the same significance as defined above, and R^9 is hydrogen, a cycloalkyl having 3 to 12 carbon atoms or a

substituted cycloalkyl having 3 to 12 carbon atom which is substituted with 1 to 3 alkyl groups having 1 to 5 carbon atoms;

5) $-C_tH_{2t}-CH=C(R^{10})R^{11}$, wherein C_tH_{2t} has the same significance as defined above, and R^{10} and R^{11} represent hydrogen, methyl, ethyl, propyl or butyl; or

6) $-C_uH_{2u}-C\equiv C-R^{12}$, wherein u is an integer of 1 to 7, C_uH_{2u} is a straight or branched alkylene and R^{12} is a straight alkyl having 1 to 6 carbon atoms);

E represents hydrogen or OR^{13}, wherein R^{13} is hydrogen, an acyl having 1 to 12 carbon atoms, an aroyl having 7 to 18 carbon atoms, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms; or a salt thereof

and optionally the composition is formulated with at least one additional component selected from the group consisting of vegetable oil, fatty acid triglycerides, fatty acid esters, polysiloxanes, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen.

Claim 18. (Previously Presented) A sustained-release pharmaceutical composition according to claim 17, wherein the ionic compound is sodium laurylsulfate and/or sodium oleate.

Claim 19. (New) A sustained-release pharmaceutical composition according to claim 4, wherein the composition is formulated with at least one additional component selected from the group consisting of vegetable oil, fatty acid triglycerides, fatty acid esters, polysiloxanes, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen.

Claim 20. (New) A sustained-release pharmaceutical composition according to claim 19, wherein the composition is formulated with at least one additional component selected from the group consisting of soybean oil, sesame oil, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen.

Claim 21. (New) A sustained-release pharmaceutical composition according to claim 17, wherein the composition is formulated with at least one additional component selected from the group consisting of vegetable oil, fatty acid triglycerides, fatty acid esters, polysiloxanes, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen.

Claim 22. (New) A sustained-release pharmaceutical composition according to claim 21, wherein the composition is formulated with at least one additional component selected from the group consisting of soybean oil, sesame oil, hyaluronic acid or a salt thereof, hydroxypropylcellulose and atherocollagen.

The following is an examiner's statement of reasons for allowance: The prior art does not teach or suggest the instant composition consisting essentially of instant prostanoic acid derivatives, instant ionic (anionic / cationic) compounds, plus optionally at least one additional ingredient selected from fats, polysiloxanes, hyaluronic acid and salts thereof, HPC, and atherocollagen.

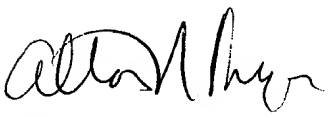
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Telephonic Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alton N. Pryor whose telephone number is 571-272-0621. The examiner can normally be reached on 8:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Alton Pryor
Primary Examiner
AU 1616